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Prevalence of Hypertension and Its Association with Tuberculosis, among HIV patients on ART in Bagamoyo District, Eastern Tanzania

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ABSTRACT

Background: Individuals living with HIV/AIDS have a higher risk of cardiovascular complications, including hypertension. We, therefore, assess the prevalence of hypertension and its association with Tuberculosis in HIV patients on ART in Bagamoyo district eastern Tanzania.

Methods: This was a cross-sectional study involving HIV-infected individuals on ART, consecutively enrolled from two selected care and treatment clinics (CTC), between March and May 2019. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mm Hg, diastolic blood pressure (DBP) ≤ 90 mm Hg or being on-ant hypertensive medication regardless of blood pressure measurement on the day of the visit.

Results: We investigated 328 HIV patients on ART, 64.6% were female, 92.68% on non-protease inhibitors, 0.61% had current TB and 14% had a history of Tuberculosis in the past 5 years. The overall prevalence of hypertension in HIV patients on ART was 29.3% and it was significant and positively associated with increasing age, obesity, family history of hypertension, and, current history of TB. However, having a history of Tuberculosis in the past 5 years was not associated with increased odds of having hypertension.

Conclusion: The prevalence of hypertension in HIV patients on ART was higher and it was associated with traditional risk factors and the current history of tuberculosis and but not with a history of Tuberculosis in the past 5 years. Regular monitoring of blood pressure is crucial among HIV/AIDS patients attending HIV outpatient clinics.

Keywords: HIV, Hypertension, ART, CTC, Tuberculosis

Abbreviations: ART: Anti-Retroviral Therapy; BMI: Body Mass Index; CTC: Care and Treatment Clinic; HIV: Human Immunodeficiency Virus; TB: Tuberculosis

INTRODUCTION

Effective use of antiretroviral therapy (ART), has greatly improved the quality of life and survival of people living with HIV/AIDS [1]. However, the incidence rate and mortality from cardiovascular risk factors including hypertension are reported to be growing up [2-4]. For example, in a recent meta-analysis study prevalence of hypertension was 34.7% among those on ART compared to 12.7% in ART naïve individuals [5]. In Tanzania, hypertension prevalence of (28.3%) in HIV patients on ART has been reported at 28.3% which is higher compared to 5.3% in HIV ART-naïve and 16.3% in HIV negative individuals [6].

Hypertension (the leading risk factor of deaths) is a growing health problem in individuals living with HIV/AIDS [7,8].

However, the contributions of HIV related factors include Tuberculosis to hypertension have not been extensively investigated in Tanzania. In addition to the traditional risk factors, hypertension in HIV patients can be attributed to, inflammation, ART toxicity and immune response [9].

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Traditional risks include risks such as increasing age, sex and increasing Body mass index [10]. However, it's unclear whether traditional risk factors may interact with HIV related factors such as Tuberculosis (TB) to increase the risk of hypertension.

Evidence exists that TB may contribute to overall cardiovascular risk including hypertension perhaps through inflammation and autoimmune processes [11,12]. Although TB is the most prevalent and severe co-infection in HIV patients [13,14], little is known about its association with hypertension in HIV patients, especially in developing countries.

Therefore, we undertook a cross-sectional study to investigate the prevalence of hypertension and its association with TB in HIV patients on ART adjusting for potential confounders. To the best level of our knowledge, this cross-sectional study is the first of its kind to investigate the association between TB and hypertension among HIV patients on ART while adjusting for confounders.

METHODS

Study design and location

We conducted a cross-sectional study involving HIV patients who were on ART between March and April 2019, in Bagamoyo district, eastern Tanzania. The district is located in the coastal region with an HIV prevalence rate of 6.4% [15]. Data were collected from 2 public clinics which were purposely selected based on their relatively large size and presence of patient's record database (computer-based record system). These clinics provide services to individuals living with HIV/AIDS based on national HIV/AIDS guidelines [16].

The inclusion criteria were being HIV positive, aged above 18, on ART, who gave consent for participation. Women who reported to be pregnant and those on contraceptive pills were excluded. The patients were then consecutive enrolled until the target sample size of 328 was achieved.

Blood pressure measurement

Blood pressure was measured in the right arm, using a mercury sphygmomanometer of appropriate size, with individual participants sitting in a relaxed position and upright position [17], two readings were taken 10 min apart and an average of two readings was used. Hypertension was defined as systolic blood pressure (SBP) of ≥ 140 mm Hg, diastolic blood pressure (DBP) of ≥ 90 mm Hg [17] or taking ant-hypertensive medications regardless of blood pressure findings.

Anthropometric measurement

Body weight (accuracy of 0.1 kg) was measured using Seca patients weighing machines with individual participants at minimal clothes and wearing no shoes. Body height was measured using a stadiometer (accuracy of 0.1 cm)

participant wearing no shoes. Body mass index (BMI) was calculated using the formula: weight in kilogram (kg) divided by the square of height in meters (kg/m^2). BMI was categorized and defined using the WHO protocol as follows, underweight $<18.5 \text{ kg/m}^2$, normal body weight $18.5\text{--}24.9 \text{ kg/m}^2$, overweight $25\text{--}29.9 \text{ kg/m}^2$ and obese $\geq 30 \text{ kg/m}^2$ [18].

Collection of socio-demographic and HIV related information

The study used a structured questionnaire administered by trained health care workers (nurses and doctors) was used to gather information with respect to participants' socio-demographic, family history of hypertension, current history of tuberculosis and history of tuberculosis in the past 5 years.

The following information was extracted directly from patient record card or computerized patient database system: Duration since HIV diagnosed, Recent CD4+ cell count, the current class of ART medication, individual combination therapy and duration on ART medication.

Definition of terms

Recent CD4+ cell count was defined as the amount of CD4+ T cell count which was measured in the past 6 months. Current TB was defined as currently being on anti-TB medication after sputum analysis or chest radiography. History of TB in the past 5 years was defined as being on anti-TB medication for at least 6 months within the last 5 years.

Study variables

The outcome variable of interest was hypertension defined as blood pressure $\geq 140/90$ mm Hg or being on ant-hypertensive medication. Exposure variables of interest during the analysis were current TB/HIV co-infection and the history of TB in the past 5 years.

Data management and analysis

Data was collected using a study questionnaire, then coded using a codebook followed by the manual entrance in an excel sheet. Before data entry in the excel sheet completed questionnaire was reviewed for completeness and clarity. Before data analysis, another review was done for errors, missing data, and inconsistencies. The analysis was done using Stata software version 13.

We included 328 participants in the final analysis and 33 participants had missing data regarding the recent CD4+ cell count. Recent CD4+ cell count was defined as the one which was taken within the last 6 months. In 33 participants with missed data on CD4+ cell count, they had CD4+ cell count either not taken at all or taken in a period of more than 6. A descriptive analysis (percentage) was used to summarize the data. Logistic regression, both univariate and multivariate analysis was performed to establish the risk factors of hypertension. In the multivariate analysis, we included

factors with $p\text{-value} \leq 0.005$, age, sex and the current class of ART.

ETHICAL APPROVAL

The study was approved by institutional review of the Ifakara Health Institute, Bagamoyo district executive director office as well as the authority of the respective health facility. Written informed consent was obtained from all study participants prior to study procedures.

RESULTS

Table 1 summarizes the socio-demographic and TB characteristics of the participants. We included 328 HIV infected individuals who were on ART for the analysis. Out of all participants, 212 (64.6%) were female and 116 (35.4%) male. In the description of the age categories, 132

(40.24%), 151 (46.06%) and 45 (13.72%) were individuals aged 18-39, 40-59 and ≥ 60 , respectively. Out of 328, 89 (25%) of the participants were either obese or overweight. Current alcohol drinker and smoking cigarettes were observed in 42 (12.8%) and 17 (5.18%), respectively.

Out of 328, 2 (0.61%) patients had HIV/TB co-infected and 46 (14%) of patients had a history of TB in the past 5 years (**Table 1**). There were 304 (92.68%) patients on non-protease inhibitors and 24 (7.32%) on protease inhibitors, with the majority of patients 285(86.89%) were on Tenofovir-based combination therapy and the rest were either on Zidovudine based combination therapy or Atazanavir (**Table 1**). Data on CD4+ cell count in the last 6 months was available in 25 (8.47%), 75 (25.42%), 75 (25.42%) and 120 (40.68%) patients had CD4+ cell count, <100 , 100-349, 350-499 and ≥ 500 , respectively (**Table 1**).

Table 1. Socio-demographic and clinical profile of the participants.

Factors of interest ^a	N (%)
Overall	328
Age (Years)	
18-39	132 (40.24)
40-59	151 (46.06)
≥ 60	45 (13.72)
Sex	
Female	212 (64.63)
Male	116 (35.37)
Occupation	
Peasant	213 (64.94)
Others	115 (35.06)
Current social behavior	
Alcohol drinker	42 (12.80)
Smoking cigarette	17 (5.18)
BMI (kg/m²)	
Underweight (<18.5)	46 (14.02)
Normal weight (18.5-24.9)	193 (58.84)
Overweight (25-29.9)	51 (15.55)
Obese (≥ 30)	38 (11.59)
Recent CD4 +cell count(cell/μl)^b	
<100	25 (8.47)
100-349	75 (25.42)
350-449	75 (25.42)

≥ 500	120 (40.68)
Current class of ART	
Protease inhibitors	24 (7.32)
Non-protease inhibitors	304 (92.68)
Individual cART	
Zidovudine	19 (5.79)
Tenofovir	285 (86.89)
Atazanavir	24 (7.32)
History of chronic disease	
Family history of hypertension	41 (12.50)
Current TB/HIV co-infections	2 (0.61)
History of TB in past 5 years	46 (14.02)

ART: antiretroviral therapy; BMI: Body Mass Index; cART: Combination Antiretroviral Therapy; CD4: Cluster of Differentiation 4; HIV: Human Immune Deficiency Virus; TB: Tuberculosis

^afactors are expressed as a percentage

^b33 missing data for this variable

In our current study, the overall prevalence of hypertension in HIV patients on ART was 96 (29.3%). According to gender, the prevalence was 33 (28.5%) in males and 63 (29.7%) in females (**Table 2**). Regarding TB infection, the prevalence of hypertension was 1 (50%) in those with current TB/HIV and 15 (32.6%) in those with a history of TB in the past 5 years (**Table 2**).

Table 2. Socio-demographic and clinical characteristics associated with hypertension in HIV patients.

Factors of interest ^a	Hypertensive ^b N (%)	Non- hypertensive N (%)	TOTAL
Overall	96 (29.3)	232 (70.7)	328
Age (Years)			
18-39	22 (16.7)	111 (83.3)	132
40-59	50 (33.1)	101 (66.9)	151
≥ 60	24 (53.3)	21 (46.7)	45
Sex			
Female	63 (29.7)	149 (70.3)	212
Male	33 (28.5)	83 (71.6)	116
Occupation			
Peasants	63 (29.6)	150 (70.4)	213
Others	33 (28.7)	82 (71.3)	115
Current social behavior			
Alcohol drunker	13 (39.1)	29 (69.1)	42
Smoking cigarette	7 (41.2)	10 (58.8)	17
BMI (kg/m²)			
Underweight (<18.5)	2 (4.4)	44 (95.6)	46

Normal weight (18.5-24.9)	53 (27.5)	140 (72.5)	193
Overweight (25-29.9)	20 (39.2)	31 (61.8)	51
Obese (≥ 30)	21 (55.3)	17 (44.7)	38
Recent CD4+ cell count(cell/μl)			
<100	7 (28)	18 (72)	25
100-349	23 (30.7)	52 (69.3)	75
350-449	22 (29.3)	53 (70.7)	75
≥ 500	36 (30.0)	84 (70.0)	120
Current group of ART			
Protease inhibitors	3 (12.5)	21 (87.5)	24
Non-protease inhibitors	93 (30.6)	211 (69.4)	304
Individual cART			
Zidovudine	8 (42.1)	11 (57.9)	19
Tenofovir	85 (29.4)	204 (70.6)	289
Atazanavir	3 (15)	17 (85)	20
History of chronic disease			
Family history of hypertension	20 (48.8)	21 (51.2)	41
Current TB/HIV co-infections	1 (50.0)	1 (50.0)	2
History of TB in past 5 years	15 (32.6)	31 (67.4)	46

ART: Antiretroviral Therapy; BMI: Body Mass Index; cART: Combination Antiretroviral Therapy; CD4: Cluster of Differentiation 4; HIV: Human Immune Deficiency Virus; TB: Tuberculosis

^afactors are expressed as percentage

^bhypertensive defined as systolic BP ≥ 140 , diastolic BP ≥ 90 after an average of two readings taken at least 10 min and current use of hypertensive medications regardless of BP findings

^c33 missing data for this variable

In univariate logistic regression analysis, the factors that were significantly associated with increased odds of having hypertension were: increasing age, higher BMI, family history of hypertension and non-protease inhibitors (**Table 3**). The odds for hypertension were highest among individuals ≥ 60 years of age, odds ratio 5.71 (2.72-12.01) <0.001 and those 40-59 years of age had an odds ratio of 2.48 (1.40-4.37) <0.001 (**Table 3**). Moreover, regarding body mass index obese hold the highest odds ratio of 3.3 (1.60-6.66) <0.001 and overweight 1.70 (0.89-3.25) <0.001 (**Table 3**). A family history of hypertension and non-protease inhibitors had an odds ratio of 2.64 (1.36-5.15) <0.001 and 3.09 (0.89-10.6) <0.001 , respectively (**Table 3**).

Table 3. Univariate analysis of factors associated with hypertension (N=328).

Factor of interest	n	Odds ratios (95% CI)	P value
Age (years)			
18-39	132	1	<0.001
40-59	151	2.48 (1.40-4.37)	
≥ 60	45	5.71 (2.72-12.01)	
Sex			
Male	116	1	0.810
Female	212	1.06 (0.65-1.78)	
Occupation status			
Peasant	213	1	0.867
Non peasant	115	0.96 (0.58-1.58)	
Current social behavior			
Alcohol drunker			0.80
No	286		
Yes	42	1.10 (0.54-2.21)	
Smoking cigarette			0.282
No	311	1	
Yes	17	1.75 (0.64-4.73)	
BMI (kg/m ²)			
Normal weight (18.5-24.9)	193	1	<0.001
Underweight (<18.5)	46	0.12 (0.28-0.51)	
Overweight (25-29.9)	51	1.70 (0.89-3.25)	
Obese (≥ 30)	38	3.3 (1.6-6.66)	
Recent CD4+ cell count (cell/μl) ^d			
<100	25	1	0.995
100-349	75	1.13 (0.42-3.09)	
350-499	75	1.07 (0.39-2.91)	
≥ 500	120	1.10 (0.42-2.87)	
Current group of ARV medications			
Protease inhibitors	24	1	0.043
Non- protease inhibitors	304	3.09 (0.89-10.6)	
Individual cART			
Zidovudine	19	5.09 (1.12-23.14)	0.0712
Tenofovir	289	2.98 (0.86-10.24)	

Atazanavir	20	Omitted	
History of chronic diseases			
Family history of hypertension			0.005
No	41	1	
Yes	287	2.64 (1.36-5.15)	
Current TB/HIV co-infections			0.538
No	326	1	
Yes	2	2.42 (0.15-39.28)	
History of TB in past 5 years			0.595
No	282	1	
Yes	46	1.2 (0.62-2.34)	

ART: Antiretroviral Therapy; BMI: Body Mass Index; cART: Combination Antiretroviral Therapy; CD4: Cluster of Differentiation 4; HIV: Human Immune Deficiency Virus; TB: Tuberculosis

b=hypertensive defined as systolic BP ≥ 140 , diastolic BP ≥ 90 after an average of two readings taken at least 10 min and current use of hypertensive medications regardless of BP findings

d=33 missing data

In the multivariate analysis, HIV related factors that were independently associated with increased odds of having hypertension were, non-protease inhibitors 4.31 (1.16-16.03) <0.001 , current TB/HIV co-infection 3.13 (0.12-80.41) <0.001 , Zidovudine 4.66 (0.91-23.99) <0.001 and tenofovir 4.27 (1.15-15.96) <0.001 . However, recent CD4+ count and history of TB in the past 5 years were not associated with increased odds of hypertension (**Table 4**).

Table 4. Multivariate analysis of factors associated with hypertension (N=328).

Factor of interest	n	Adjusted odds ratios (95% CI)	P value
Age (years)			
18-39	132	1	<0.001
40-59	151	3.40 (1.80-6.41)	
≥ 60	45	9.25 (3.96-21.60)	
Sex			
Male	116	1	<0.001
Female	212	0.78 (0.43-1.40)	
Occupation status			
Peasant	213	1	<0.001
Non peasant	115	1.24 (0.69-2.24)	
Current social behavior			
Alcohol drinker			<0.001
No	286	1	
Yes	42	1.29 (0.57-2.92)	
Smoking cigarette			<0.001
No	311	1	

Yes	17	2.12 (0.65-6.90)	
BMI (kg/m ²)			
Normal weight (18.5-24.9)	193	1	<0.001
Underweight (<18.5)	46	0.70 (0.02-0.32)	
Overweight (25-29.9)	51	1.61 (0.77-3.36)	
Obese (≥ 30)	38	3.63 (1.60-8.26)	
Recent CD4+ cell count(cell/μl) ^d			
<100	25	1	<0.001
100-349	75	0.90 (0.30-2.70)	
350-499	75	1.04 (0.34-3.16)	
≥ 500	120	1.25 (0.43-3.60)	
Current group of ART			
Protease inhibitors	24	1	<0.001
Non-protease inhibitors	304	4.31 (1.16-16.03)	
Individual cART			
Zidovudine	19	4.66(0.91-23.99)	<0.001
Tenofovir	285	4.27(1.15-15.96)	
Atazanavir	24	Omitted	
History of chronic diseases			
Family history of hypertension			<0.001
No	41	1	
Yes	287	2.73 (1.27-5.84)	
Current TB/HIV co-infections			<0.001
No	326	1	
Yes	2	3.13 (0.12-80.41)	
History of TB in past 5 years			<0.001
No	282	1	
Yes	46	1.15 (0.55-2.43)	

ART: Antiretroviral Therapy; BMI: Body Mass Index; cART: Combination Antiretroviral Therapy; CD4: Cluster of Differentiation 4; HIV: Human Immune Deficiency Virus; TB: Tuberculosis

b=hypertensive defined as systolic BP ≥ 140 , diastolic BP ≥ 90 after an average of two readings taken at least 10 min and current use of hypertensive medications regardless of BP findings

d=33 missing data

DISCUSSION

In this cross-sectional study analyzing the prevalence of hypertension and its association with TB among HIV patients, we found the prevalence of hypertension to be 29.3%. We also observed that the odds of having

hypertension were significantly associated with increasing age, obesity, and family history of hypertension and non-protease inhibitors. Current TB/HIV co-infection was found to increase the odds of having hypertension in multivariate analysis.

The high prevalence (29.3%) in our current study appears similar to that of the observed prevalence in previous studies in HIV patients [5,6]. This strengthens the evidence that the prevalence of hypertension is higher in HIV patients on ART.

We also observed factors that were significant and positively associated with increased odds of hypertension which included: increasing age, obesity and family history of hypertension. These findings are consistent with previous studies [19,20]. This supports the evidence that traditional risk factors are potential predictors of hypertension even in HIV patients.

The interaction between TB infection and hypertension in HIV patients has been reported in the literature [11]. The possible mechanism by which TB can cause hypertension is through the inflammatory process which can end up with atherosclerosis [11]. Furthermore, TB can contribute to hypertension, because it can lead to diabetes mellitus [21] and diabetes mellitus itself is the risk factor of hypertension [22]. Additionally, hypertension may occur secondarily from renal failure after TB causing extensive destruction of kidney parenchyma tissues [23]. In our current study, we found that current TB/HIV co-infection increases the odds of having hypertension 3.13 (0.12-80.41) <0.001 in multivariate analysis. This result differs from the study in Dar es Salaam Tanzania which found no significant association between current TB/HIV co-infection and hypertension [24]. However, we cannot justify the association between current TB and hypertension based on 2 patients with current TB infection which is a very small number to conclude. Therefore, in our current study, the interpretation regarding the association between current TB and hypertension in HIV patients on ART should be made with caution.

In our current study, we also found that having a history of TB in the past 5 years did not increase the odds of having hypertension, contrary to the previous study in Dar es Salaam, Tanzania which reported a protective effect of prior history of TB against hypertension [24]. An important difference to note is that in our current study we limited the history of the previous TB to within 5 years while the study by Njelekela et al. [24], had no time limit concerning the prior history of TB. We recommend further studies to investigate more about the association between TB and hypertension in HIV patients on ART.

CONCLUSION

The prevalence of hypertension in HIV patients on ART was higher and it was associated with traditional risk factors but not with the history of Tuberculosis in the past 5 years. We cannot justify the association between current TB infection and hypertension based on 2 patients with current TB infection which is a very small number to conclude.

Routine screening of blood pressure and health education, body weight control, healthy diet, physical activity should be emphasized as essential components of treatment and care of HIV patients. We recommend further longitudinal studies to explore more on the association between TB and hypertension in HIV patients.

We faced the followings limitations: being cross-sectional we cannot establish causality between selected exposure variable and outcome variable. Also, we did not include HIV-negative individuals to make a comparison between the two groups. Again we cannot justify the association between current TB infection and hypertension based on 2 patients with current TB infection which is a very small number.

Despite the mentioned limitations, this study provided important results regarding the association between TB and hypertension in HIV patients on ART, particularly in low-income countries.

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